

Appln No. 09/308,607

Amdt date February 17, 2004

Reply to Office action of October 14, 2003

REMARKS/ARGUMENTS

Claims 1 to 5 and 11 to 19, as amended, are pending. Applicant has amended claims 1 and 5, and added claim 19. Support for the amendments to claims 1 and 5, and new claim 19 can be found in the original specification at page 7, lines 11 to 18. Applicant has also amended the specification to correct a typographical error in the Examples. No new matter is presented. In view of the above amendments and following remarks, Applicant respectfully requests favorable reconsideration and a timely indication of allowance.

The Examiner rejected claims 1, 2, 5, 11, 14, 15, and 18 under 35 U.S.C. § 103(a) as allegedly unpatentable over Schumacher (DE 3835728 A1) or Reetz et al. (DE 4118752 A1) in combination with Vit et al. (U.S. Patent No. 4,693,986). Applicant respectfully traverses this rejection.

Claim 1, as amended, recites "a process for producing porous spherically-shaped bio-ceramics comprising dropping a starting material for ceramics into a low temperature medium from a thin tube having an inner diameter ranging from about 0.3 to 2 mm, followed by freeze drying in the medium and then sintering the same, wherein the starting material is obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100  $\mu\text{m}$ , a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder." As the specification discusses, it has been discovered that this process results in spherical-shaped bioceramic particles having a relatively large size, for

**Appln No. 09/308,607**

**Amdt date February 17, 2004**

**Reply to Office action of October 14, 2003**

example, about 10 mm, and having a uniform porosity. The bioceramic particles produced in accordance with the invention are particularly useful for the preparation of bone filler or other biorepair material and for impregnating a drug into the pores of the particles. Independent claim 5 has been similarly amended to recite the step of "dropping the starting material into a low temperature medium from a thin tube having an inner diameter ranging from about 0.3 to 2 mm".

The claimed process is neither taught nor suggested by the cited combination of references. Although as the Examiner states Schumacher does disclose producing particles having a size ranging from about 1 to 1000 nm by introducing a solution containing the ceramic material in a cold reactor to freeze the droplets, there are a number of deficiencies that the Examiner overlooks in his analysis.

First, Schumacher atomizes the solution before introducing it into the low temperature region. This is an inherently uncontrolled and uncontrollable process. In contrast, Applicant discloses a system for controllably introducing the solution in a dropwise fashion such that the particles can be controllably formed. Moreover, the instant invention allows for the formation of a spherical-shape freeze-dried product having a diameter of .3 to 2mm. In contrast, as is explicitly stated in Schumacher, the prior art process can only produce particles up to 1000 nm in size. Indeed, by its nature an atomization process cannot form such large particles. Moreover, the advantage obtained in the current process over the conventional

**Appln No. 09/308,607**

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"spray" process as described by Schumacher is explicitly recited in the background of the specification, which recites:

The general production process is a spray drying granulation method. The spray drying granulation method is generally used for the production of particles having a particle size of 100  $\mu\text{m}$  or less. An extremely large-sized apparatus is required for producing larger particles. . . .

However, for use as a bone filler, particles having a size of 100  $\mu\text{m}$  or more are desirable. Capital investment is required for producing this by spray investment is required for producing this by the spray drying granulation method, and therefore, the costs are increased.

(Specification, page 2, lines 6 to 30.)

In summary, the present method permits the starting slurry to be "dropped" in a controlled manner to thereby produce spherical bioceramic particles having a large uniform particle size. Schumacher nowhere teaches or suggests the claimed step of dropping a starting material for ceramics into a low temperature medium from a thin tube having an inner diameter ranging from about 0.3 to 2 mm and as such is limited to conventionally size particles of less than 1000 nm.

Likewise, Reetz discloses a conventional sintered ceramic spray-dried granulate process. As discussed above, such spraying techniques are not particularly suitable for bioceramics and are particularly ill-suited for forming the large sized particles disclosed herein. Reetz nowhere teaches or suggests the claimed step of dropping a starting material for ceramics into a low temperature medium from a thin tube having

**Appln No. 09/308,607**

**Amdt date February 17, 2004**

**Reply to Office action of October 14, 2003**

an inner diameter ranging from about 0.3 to 2 mm. The Examiner again equates the dropwise method of the current invention with the conventional spray atomization techniques disclosed in Schumacher and Reetz. Applicants strongly disagree with this suggestion. As described repeatedly throughout the specification, such spray atomization methods are limited in the uniformity and size of particles they can produce—limitations not present in the current invention.

Nor does the Vit reference address the deficiencies of either the Schumacher or Reetz references. Vit discloses a method of processing sinterable powders into sintered ceramic products, again preferably by spray-drying under heat. According to Vit's method, powder having a particle size of about 1 to 75  $\mu\text{m}$  is formed by the spraying method. Vit nowhere teaches or suggests the claimed step of "dropping a starting material" for producing ceramics. Moreover, Vit suggests using a heated method and not the low temperature method disclosed in the current specification. Indeed, it seems difficult to understand why one of skill in the art would ever combine the teachings of the Vit reference with those of either Schumacher or Reetz, which use cold reactors. Under the MPEP it is not allowed to combine references that would not function if combined. Here the Vit reference discloses a process which is anathema to that described by Schumacher and Reetz.

Accordingly, Applicants strongly disagree with the combination of the reference. Moreover, even if combined none of the references either alone or in combination disclose a process "for producing porous spherically-shaped bio-ceramics

**Appln No. 09/308,607**

**Amdt date February 17, 2004**

**Reply to Office action of October 14, 2003**

comprising dropping a starting material for ceramics into a low temperature medium from a thin tube having an inner diameter ranging from about 0.3 to 2 mm, followed by freeze drying in the medium and then sintering the same, wherein the starting material is obtained by adding, to a calcium phosphate in the form of a powder having a size of not more than 100  $\mu\text{m}$ , a 3 to 15% by weight aqueous solution of a binder in an amount of 2 to 4 times the weight of the powder" as disclosed herein.

The Examiner also rejected claims 3, 4, 12 and 13 under 35 U.S.C. § 103(a) as allegedly unpatentable over Schumacher or Reetz in combination with Vit and Urist (U.S. Patent No. 4,596,574). Applicant traverses this rejection as well.

Although the above arguments and distinctions also hold for this rejection, the Examiner cites Urist for the teaching that a composition comprising a physiologically acceptable biodegradable porous ceramic containing bone morphogenic protein (BMP) can be obtained by contacting a physiologically acceptable, biodegradable porous ceramic with a liquid containing substantially pure BMP and removing the liquid therefrom so that an effective amount of BMP is entrapped in the porous ceramic.

However, Urist does not address any of the deficiencies of Schumacher, Reetz or Vit references. Indeed, Urist fails entirely to disclose A process for producing porous spherically-shaped bio-ceramics comprising "dropping a starting material for ceramics into a low temperature medium from a thin tube", much less any of the claimed ranges of sizes of products or starting materials.

Appln No. 09/308,607

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Accordingly, none of the references teaches or suggests the claimed step of "dropping a starting material for ceramics into a low temperature medium from a thin tube having an inner diameter ranging from about 0.3 to 2 mm." Therefore, none of the references, even in combination, render unpatentable the claimed invention. Applicant therefore respectfully requests that the rejections under section 103(a) be withdrawn.

In view of the foregoing amendments and remarks, Applicant respectfully submits that pending claims are in condition for allowance, and a timely indication of allowance is respectfully requested. If there are any remaining issues that can be addressed by telephone, Applicant invites the Examiner to contact the undersigned at the number indicated below.

Respectfully submitted,

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